UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/761,534	01/16/2001	Qian Huang	0399.2006-003	5869

26161 7590 12/03/2002

FISH & RICHARDSON PC
225 FRANKLIN ST
BOSTON, MA 02110

EXAMINER
LI, BAO Q

ART UNIT	PAPER NUMBER
1648	13

DATE MAILED: 12/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/761,534	HUANG ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *1-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-35 are pending.

Election/Restrictions

1. Applicant's election without traverse of Group III, claims 26-35 in Paper No. 12 is acknowledged.

2. This application contains claims 1-25 drawn to an invention nonelected with traverse in Paper No. 12. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

3. Claims 26-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. Claim 26 is indefinite in that the metes and bounds of a portion thereof are not defined. The claim is interpreted in light of the specification; however, the limitation of the specification cannot read into the claim. If applicants wish to claim a particular fragment of a heat shock protein (hsp) please specify the molecule with a defined a sequence structure.

5. Moreover, claim 26 is unclear for using a word "joined to", which fails to define what the structure relationship between hsp with a heterologous molecule is. The word can be explained as mixing two proteins together or connecting two proteins covalently or non-covalently, or fused two proteins together by molecular engineering technique. Please use more clear language to define the relationship of the hsp with a heterologous molecule..

6. In addition, claim 26 is vague in that the metes and bounds of a heterologous molecule are not defined. The claim is interpreted in light of the specification; however, the specification does not teach what the definition of a heterologous molecule is. Because there are many molecular that is heterologous to hsp and is able to join with hsp, is Chitosan intended? or HIV p24 antigen intended? The heterologous molecule is a DNA molecule or protein or peptide or chemical compound? The claim should point out which kind of a heterologous molecule is intended. This affects the dependent claims 27-35.

7. Claim 27 is unclear because a portion and an ATP binding domain are not defined. The claim is interpreted in light of the specification; however, the specification does not teach what the definitions of a portion and an ATP binding5domain are. Claim should point out a precise sequence structure that encodes the ATP binding domain and a precise flanking region that is intended as a portion of an ATP binding domain in the claim.

8. Claim 31 is vague and indefinite for using a relative word of " derived". Since the specification does not provide a standard for ascertaining the requisite degree of derivation and the term of "derivation" has many interpretations, one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. Therefore the claim is considered as indefinite.

9. Claim 32 is unclear to define which half of the ATP binding domain is intended. Is 5' N-terminal half intended or 3' C-terminal half intended? Please clarify.

10. Claim 34 is unclear in that the metes and bounds of conserved amino acid are not defined. The claim is interpreted in light of the specification; however, the specification does not teach the definition of a conserved amino acid and fails to disclose which amino acid residue(s) is a conserved amino acid.

11. In addition, claim 34 is further confusing for using an indefinite language "at least", which fails to define the structure of the claimed protein. Since there is no given upper limitation of the substitution, is 100% conserved amino acid residues substitution intended? Therefore, claim is considered indefinite.

Claim 35 is vague in that the word "comprises" used here is a relative word, which fails to define what exclusively the portion of the ATP binding domain is consisted of. If Applicants wish to claim a fusion protein, in which the portion of mycobacterium tuberculosis hsp70 is exclusively made from the amino acid residues 161-370, please use more defined language , such as "consist of" to clearly define the distinctive structure of the hsp in the claimed fusion protein.

Claim Rejections - 35 USC § 112

12. Claims 26-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for having a fusion protein comprising M Bacterium tuberculosis hsp70 or fragments of the hsp70 (fragment I consisting of aa 1-166; fragment II consisting of aa 163-370;

fragment III consisting of aa 360-517 and fragment IV consisting of aa 510-625), which are fused with OAV polypeptide comprising the T cell epitope of VSV and full-length mycobacterial hsp65 full fused with the P1 polypeptide, wherein only the full length hsp fusion protein and fragment II hsp70 function as an effective antigen epitope chaperons to delivery the immune epitope to the MHC molecule, does not reasonably provide enablement for having any or all hsp fusion protein comprising any or all length of a hsp having at least half or 1-50% conserved amino acid residue substitutions in ATP biding domain or only half of ATP binding domain, which function as an effective antigen epitope chaperon to induce a CTL response. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

13. The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art would undue experimentation (See United States v. Theketronic Inc., 8USPQ2d 1217 (fed Cir. 1988). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. Theses factors were outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and gain in re Wands, 8USPQ2d 1400 (Fed. Cir. 1988). These factors are analyzed as following:

1) & 2). Sate of art and unpredictability of the art.

Heat shock proteins (hsp), which function as a chaperon for delivering an epitope of an antigen to the MHC molecule to induce the antigen specific CTL immune response, is known in the art. This chaperoning activity is relayed on the ATPase activity of hsp and the specific epitope binding pocket is a given hsp sequence. However, if the ATP binding site of hsp or some conserved sequences of the epitope binding pocket are not present, the hsp will not effectively work as a chaperon to delivery the antigen epitope to the MHC molecule for inducing an immune response. Therefore, a fusion protein made by any or all hsp fragment with any deletion or substitutive mutations in the conserved ATP binding domain or epitope binding pocket is functionally unpredictable as evidenced by Geluk et al. (J. Immunol. 1992, Vol. 149, pp. 2864-2871). For example, they have studied the interactions between hsp65 p4-13, HLA-DR17 and four different TCRs, they found that amino acids I at position 5 and D at poison 8 are critical HLA-DR17 biding. At T cell level, residues 6(A), 7(Y) and 9(E) were identical as

important residues for all four clones. Tyrosine (Y) is known to play a critical role in the number of T cell epitopes, which often shows a limited replaceability and could only be replaced by phynylalanine (F) (See lines 8-32 on col. 2, page 2868). The unpredicatblity of mutation of the ATP binding site of hsp is also demonstrated by Applicants own disclosure because specification shows that only the fusion proteins, which comprising hsp70 amino acid residues from 165 to 370, are able to induce a similar immune response as compared to the full length of the hsp70.

3) & 4) Number of working examples and amount of guidance.

Specification of present application is deficient fro teaching any or all hsp having only half of ATP binding domain or having at least half or 1-50% conserved amino acid substitution in the ATP binding activity is able to work as a effective chaperon for delivering the immune epitope to the MHC molecule and inducing a antigen specific CTL response, more preferably in an CD4 independent manner.

Specification does not teach which domain is the hsp ATP biding domain, which half of the ATP binding domain is intended? Which amino acid residue is a conserved amino acid residue, which 1-50% of conserved amino acid residues should be substituted, and which amino acid is suitable for the substitution?

Specification does not have an adequate guidance for dosing the claimed invention either.

5) Scope of the claims.

The scope of the claimed invention read broadly on any or all fusion polyeptide comprising any or all length of a hsp having at least half or 1-50% conserved amino acid residue substitutions, wherein the hsp part of the fusion protein still possess the ATP binding ability and full file the function as an effective antigen epitope chaperon to induce a CTL response.

6) & 7) Nature of the invention and level of the art.

Nature of the invention is related molecular modeling the hsp molecule functionally used for antigen epitope chaperon to induce CD4 independent immune response. The level of the skill in generating or studying every amino acid in ATP binding domain function by substituting each amino acid in the domain and testing the function of chaperon activity is quit high and unpredictable.

Given the above analysis of the factors, which the courts have determined, are critical in asserting whether a claimed invention is enabled, it must be considered that the skilled artisan

would have to conduct undue and excessive experimentation in order to practice the claimed invention.

Claim Rejections - 35 USC § 112

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 32-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the instant case, the specification only presents the fusion proteins made by full length hsp70 or fragment of hsp70 1-166, or 161-370, 360-517 or 510-625 fused with a portion of OVA (amino acid 230-359) and hsp65 fused with P1 polypeptide, wherein the fusion proteins that are enable to induce CD4 independent CTL immune response are hsp70 or hsp 65 full length or hsp70 fragment of 165-170. However, the specification is rather deficient for teaching when how to make a fusion protein by using a truncated hsp with half ATP binding domain or at least 1-50% of substituted conserved amino acids in the ATP binding domain. Specification even does not teach which domain is the hsp ATP biding domain.

This function of hsp work as a chaperon is relayed on the ATPase activity of a hsp and the specific epitope binding pocket of a given hsp. However, if the ATP binding site of hsp or some conserved sequences of the epitope binding pocket are not present, the hsp will not effectively work as a chaperon to delivery the antigen epitope to the MHC molecule for inducing an immune response. Therefore, a fusion protein made by any or all hsp fragment or any mutation of amino acid in its conserved binding sequence is functionally unpredictable as evidenced by Geluk et al. (J. Immunol. 1992, Vol. 149, pp. 2864-2871). For example, they have studied the interactions between hsp65 p4-13, HIL-DR17 and four different TCRs. They found that amino acids I at position 5 and D at poison 8 are critical HLA-DR17 biding residues. At T

cell level, residues 6(A), 7(Y) and 9(E) were identical as important residues for all four clones. Tyrosine (Y) is known to play a critical role in the number of T cell epitopes and often shows a limited replaceability and it could only be replaced by phynylalanine (F), which contain a large aromatic group in its side chain (See lines 8-32 on col. 2, page 2868).

Because the specification does not teach or describe domain is the ATP binding domain for any or all heat shock proteins, which half of the ATP binding domain is intended, which amino acid in any or all hsp is the conserved amino acid residues in the ATP binding domain, which 1-50 conserved amino acid residues are suitable for the substitution, the claimed invention does not have the possession for having any or all fusion protein made by any or all hsp with half ATP biding domain or at least 1-50% conserved amino acid residues substituted in the ATP binding domain.

See *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed, Cir. 1997):

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention ....

and at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.

Also, please see *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by

> its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

The case law of *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016, which teach that the disclosure of a process for obtaining cDNA and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism. 35 USC 112 requires inter alia that "a patent specification contain a written description of the invention and the manner and process of making and using it in such full clear and concise terms as to enable one skilled in the art to make and use the invention". Case law has made it clear that the requirements for a "written description" and an "enabling disclosure" are separate. For example, where a specification contains sufficient information to enable a skilled chemist to produce a particular compound because it gives detailed information on how to produce analogous compounds but it makes no reference to the compound in question, the "written description" requirement has not been met even though the description may be enabling.

Double Patenting

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

17. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

18. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 26-31 and 35 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-92 of U.S. Patent No. 6,338,952 B1) in view of Suzue et al. (P.N.A.S. USA, 1997, Vol. 94, pp. 13146-13151)

20. The claimed invention is drawn to a composition comprising a heat shook protein (hsp) or portion of heat shock poring, joined to a heterologous molecule, wherein the hsp is a mammalian hsp or mycobacterial hsp, preferably is mycobacterium tuberculosis, mycobacterium leprae or mycobacterium bovis (m. bovis) . The portion of the hsp is preferably a portion of an ATP binding domain of a hsp.

21. Patent 952B1 claims an isolated fusion protein and a composition comprising the fusion protein, wherein the fusion protein is made from a full length of hsp joined to a heterologous protein or peptide via a peptide bond, wherein the hsp is a full length hsp, including the hsp70 family, the hsp60 family, the groEs family, the Dnal family, the hsp90 family and the small molecular stress proteins. The fused heterotopous protein or peptide is a viral protein antigen or viral peptide antigen, or cancer antigen. Patent 951B1 does not claim that the hsp contains an ATP binding domain. However, it is well known in the art that all hsp contains an ATP binding domain, the hsp as disclosed in Patent 952B1 is a full-length hsp, it inherently contains this ATP binding domain. This common structural characteristics of hsp are well documented in the art before the current application is filed. The support of this is substantiated by the evidence taught by Suzue et al. They teach the kinetics of hsp70-substrate binding is governed by the ATP binding and ATPas activity of hsp70. The combination of peptide and ATP binding function of hsp70 may be involved in the efficient transfer of antigenic peptides to the MHC class I antigen presentation pathway (see lines 43-48 on col. 2 of page 13150)

22. Therefore, it would have been obvious for applicants to claims a hsp fusion protein comprising the ATP binding domain to ensure the functional chaperon activity of the hsp fusion protein.

23. Although the claims of the patent 925B1 read wordily different from the claimed invention in the present application, the scope of the claimed invention is overlapping.

Claim Rejections - 35 USC § 102

24. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 26, 28-31 and 35 are rejected under 35 U.S.C. 102(e) as being anticipated by Young (US Patent No. 6,338,952B1).

Patent 952B1 claims an isolated fusion protein and a composition comprising the fusion protein, wherein the fusion protein is made from a full length of hsp joined to a heterologous protein or peptide via a peptide bond, wherein the hsp is a full length hsp, including the hsp70 family, the hsp60 family, the groEs family, the Dnal family, the hsp90 family and the small molecular stress proteins. The fused heterologous protein or peptide is a viral protein antigen or viral peptide antigen, or cancer antigen. Patent 951B1 does not claim that the hsp contains an ATP binding domain (See claims 1-94). Therefore, the claimed invention is anticipated by the cited reference.

25. Claims 25-30 are rejected under 35 U.S.C. 102(e) as being anticipated by Sirivastava P. (US Patent No. 6,030,618A).

26. Sirivastava P. claims a composition comprising an immunocomplex of a heat shock protein noncovalently bound to an antigenic peptide, wherein the heat shock protein is selected

from mammalian heat shock protein hsp70, hsp90, and hsp96, and wherein the antigenic peptide is selected from viral antigen and cancer antigens. Although Sirvastava does not explicitly teach that the hsp he disclosed contains the ATP binding domain, the full-length hsp inherently contains the ATP biding domain. Therefore, the claimed invention is anticipated by the cited reference.

27. Claims 26 and 28-31 are rejected under 35 U.S.C. 102(e) as being anticipated by Rappuoli et al. (US Patent 6,403,009B1).

28. Rappuoli et al. disclosed a conjugated compound comprising a portion of at least 11-15 amino acid residues of a heat shock protein selected from the group consisting of M. Bovis BCG GroEI-type 65 kDA heat shock protein and recombinant M. Tuberculosis DnaK-type 70 kDa heat shock protein, said conjugated compound also comprising at least one capsular oligosaccharide or capsular polysaccharide, or immunogenic portion thereof (claim 1-11).

29. Claims 26-30 and 35 are rejected under 35 U.S.C. 102(e) as being anticipated by wallen et al. (US Patent NO. 6,455,493B1).

30. Wallen et al. disclose a heat shock protein immunotoxin comprising a heat shock protein, a toxin comprising a peptide. Although Wallen et al. de not explicitly teach that the hsp he disclosed contains the ATP binding domain, the full-length hsp as he disclosed inherently contains the ATP biding domain (See claims 1-8). Therefore, the claimed invention is anticipated by the cited reference.

Claim Rejections - 35 USC § 102

31. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

32. Claims 26-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Ciupitu et al. (J. Exp, Med. 1998, Vol. 187, p. 685-691).

33. Ciupitu et al. disclose a composition made by a lymphocytic choriiomenigitis virus peptide mixed wit human heat shock protein hsp70 (see entire document). Although Ciupitu et

al. does not explicitly teach that the hsp as disclosed in the publication contains the ATP binding domain, the full-length hsp as it is disclosed in the paper inherently contains the ATP biding domain. Therefore, the claimed invention is anticipated by the cited reference.

34. Claims 26-31 and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Young (WO 98/35705).

35. Young disclose a recombinant fusion protein made by hsp 70 of M. tuberculosis or heat shock protein selected from nonhuman mammalian heat shock proteins, insect heat shock protein and fugal heat shock protein and mammalian heat shock protein, which is coupled to OVA comprising viral peptide SIINFEKL or RGYVYOQGL of vesticular stomatitis virus (VSV) respectively or coupled to the moiety selected from group consisting of protein, peptides, lipids, carbohydrates, glycoproteins and small organic molecules (Claims 1-25 and lines 20 on page 16 through line 9 on page 18), wherein the hsp70 contains the ATP binding domains (lines 5-22 on page 28). Therefore, the claimed invention is anticipated by the cited reference.

36. Claims 26-31 and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Suzue et al. (P.N.A.S. USA, 1997, Vol. 94, pp. 13146-13151).

37. Suzue et al. teach a recombinant fusion protein made by hsp 70 of M. tuberculosis fused with OVA comprising viral peptide SIINFEKL or RGYVYOQGL of vesticular stomatitis virus (VSV) respectively, wherein the hsp70 is purified by ATP affinity chromatography. This fusion protein is used for inducing an antigen specific immune response in H-2b mice through MHC class I molecule (see entire document). Therefore, the claimed invention is anticipated by the cited reference.

38. Claims 25-30 are rejected under 35 U.S.C. 102(e) as being anticipated by Sirivastava et al. (WO 95/24923A2).

39. Sirivastava et al. disclose a composition comprising an immunogenic stress protein-peptide complex. The said stress protein is a member of the stress protein families selected from the group consisting of Hsp60, Hsp70 and Hsp90. The said peptide is selected from the group consisting of virus, bacteria, protozoa and an intracellular parasite. The composition further comprises a pharmaceutical acceptable carrier and a cytokine. The stress protein is harvested in the presence of ATP. The composition is used for inducing an antigen specific immune response (See claims 1-36). Therefore, the claimed invention is anticipated by the cited reference.

40. Claims 25-31 and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Barrios et al. (Eur. J. Immunol. 1991, vol. 21, pp. 2297-2302).

41. Barrios et al. teach a mycobacterium bovis BCG 65 (GroEL-type) hsp (hspR65) and mycobacterium tuberculosis 70-kD (DnaK-type) hsp (hsp70R) are expressed by recombinant E Coli and purified by ATP chromatography column. The Rhsp65 and hspR70 are coupled with (NANP)40 synthetic peptide respectively. The coupled hspR70 or hspR65is injected into mice to see an immune response (See entire document). Therefore, the claimed invention is anticipated by the cited reference.

42. Claims 25-31 and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Roman et al. (Immunology 1996, Vol. 88, pp. 487-492).

43. Roman et al. teach a hsp70 isolated from a recombinant strain of E coli over expressing DANK gene from M tuberculosis and purified from ATP agarose is non-covalently bound to a synthetic peptide, wherein the hsp70 comprises a ATP binding domain. Therefore, the claimed invention is anticipated by the cited reference.

44. Claims 26-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Ciupitu et al. (WO 93/17712A2).

45. Ciupitu et al. disclose an compound comprising oligosaccharide of meningococci C group complex with a heat shock protein selected from M bovis BCG GroEL-type 65kDa (hspR65) and recombinant tuberculosis DanK-type hsp70Da (hspR70) (Claims 1-9). Although Ciupitu et al. does not explicitly teach that the hsp contains the ATP binding domain, the full-length hsp is inherently contains the ATP biding domain. Therefore, the claimed invention is anticipated by the cited reference.

46. Claims 26, 28, 29, 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Cohen et al. (WO 95/31994A1).

47. Cohen et al. disclose a conjugated immunogenic antigen complex comprising a synthetic peptide carrier derived from the E coli hsp65 (GroEL) and an immunogenic antigen wherein the hsp65 only comprises a portion of hsp65 corresponding to position of 435-453 and the immunogenic antigen is a polysaccaride of a bacterium. The immunogenic complex is used for inducing an immure response to the specific antigen of said bacterium polysaccaride. Therefore, the claimed invention is anticipated by the said reference.

48. Claims 26-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Lee et al. (WO 98/23735A1).

49. Lee et al. disclose a vaccine composition comprising an antigen and a stress protein, wherein the mycobacterial stress protein is selected from macobacterial hsp65 and hsp71. The mycobacterial stress protein and antigen is expressed as a fusion protein, wherein the stress protein can be a protein having a n amino acid sequence sufficiently homologous to the amino acid sequence of the mycobacterial stress protein to induce the immune response and the immunogenic antigen is an antigen of influenza virus selected from the group consisting of hemagglutinin, nucleoprotein and neuramindase. Therefore, the claimed invention is anticipated by the said reference.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 703-305-1695. The examiner can normally be reached on 8:00 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bao Qun Li
November 22, 2002

James C. Housel 12/2/02
JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600